

Fig. 1

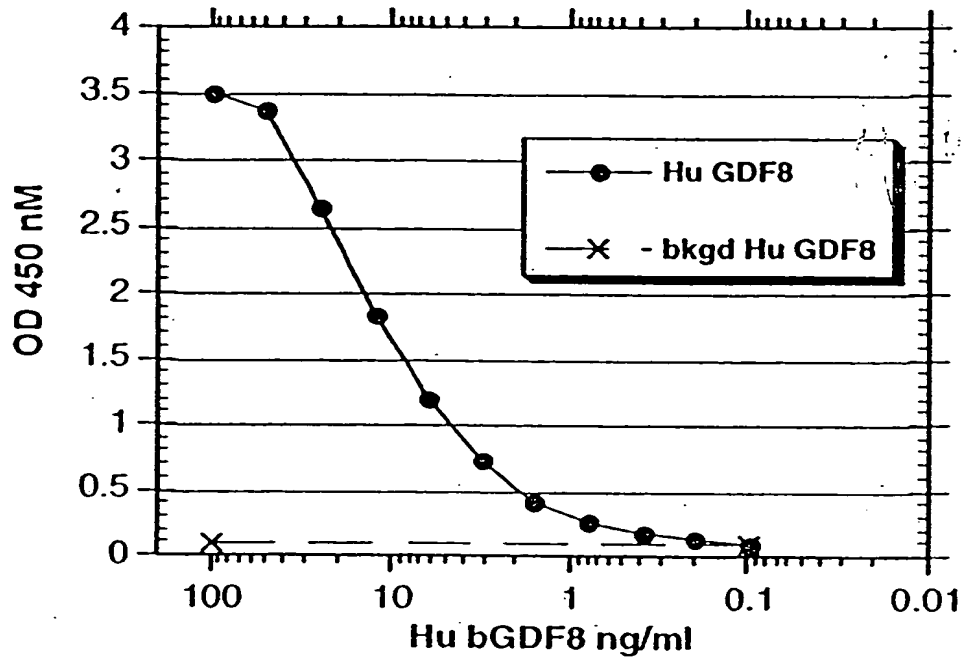


Fig. 2

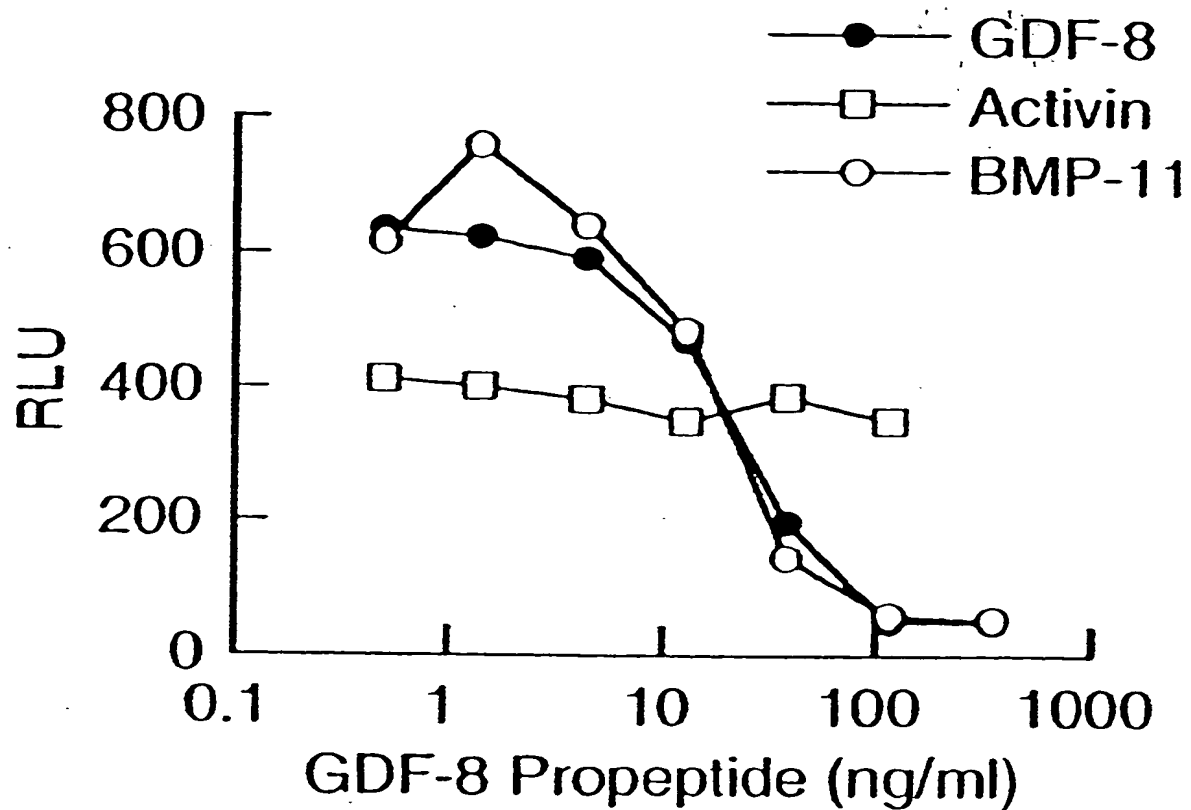


Fig. 3

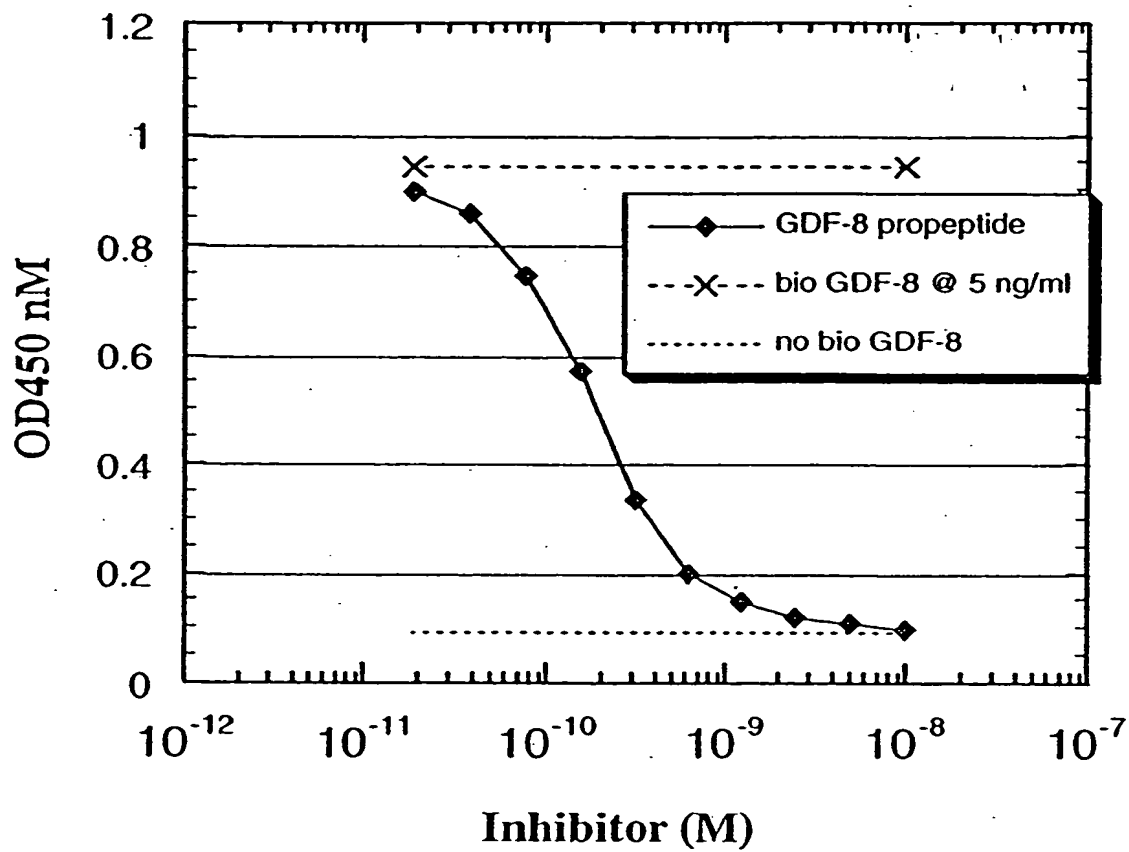


Fig. 4

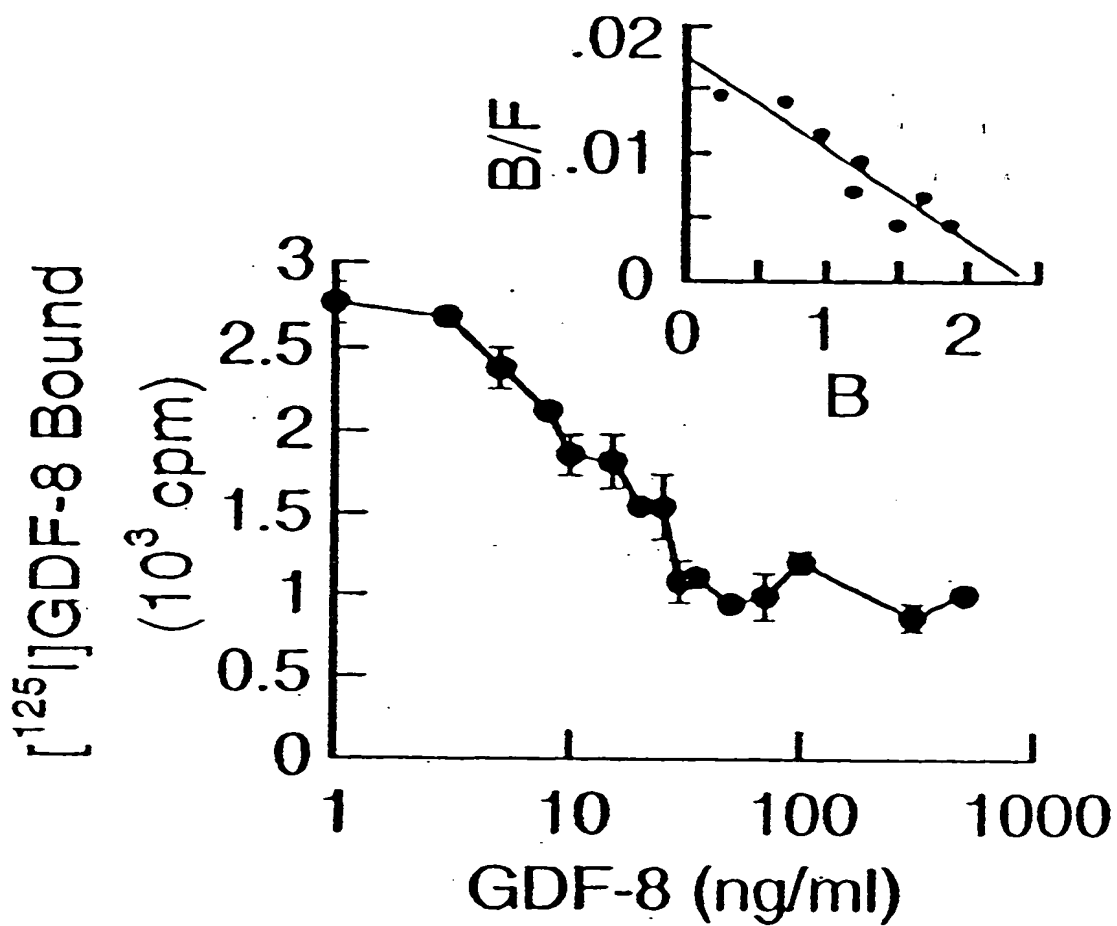


Fig. 5

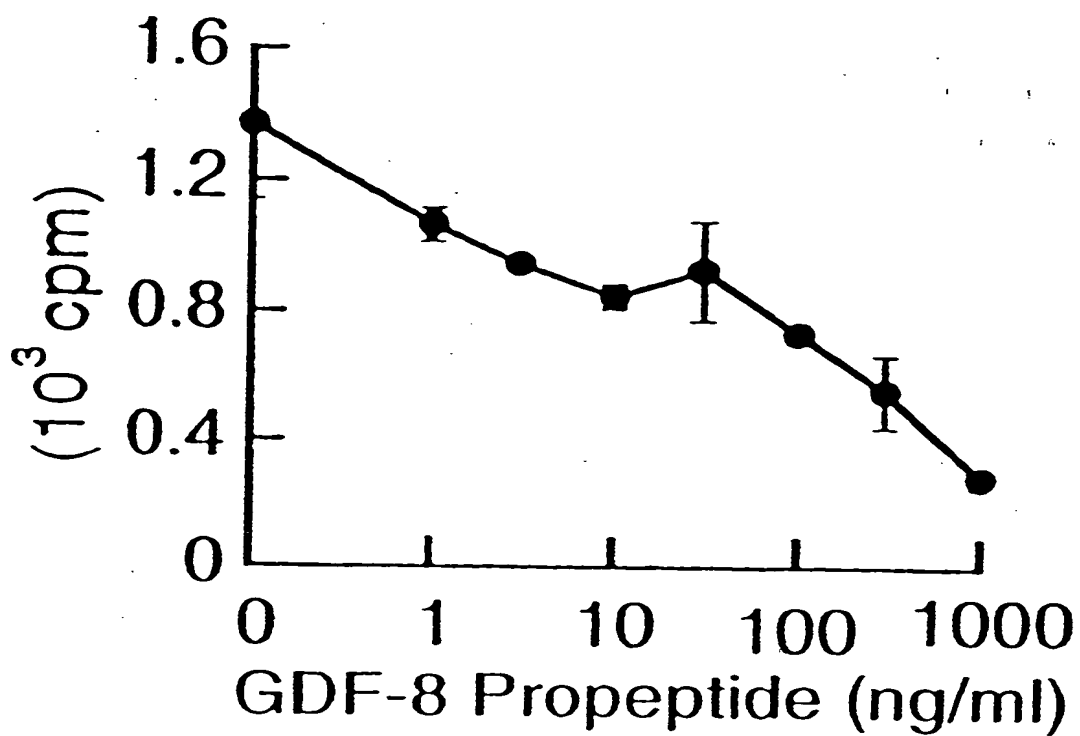


Fig. 6

NEGS	PKRS	EPRG	PGK
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Secretory Mu GDF-8 propeptide Mu IgG2a Fc
leader

MMQKLQMYVYIYLFMLIAAGPVDLNEGSEEREENVEKEGLCNACAWRQNTSYSRIEAIKIQLSKLRLET
APNISKDAIRQLLPRAAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIIITMPTESDFLMQADGKPKC
CFFKFSSKIQYNKVVAQQLWIYLRPVKTPTTVFVQILRLIKPMKDGTTRYTGIRSLKLDMSPGTGIWQSI
DVKTVLQNLWKQPESNLIGIEIKALDENGHDLA VTFPGPGEDGLNPFLEVKVTDTPKRSEPRGPTIKPCP
PCKCPAPNLEGGPSVFIFPPKIKDVLMSLSPIVTCVVDVSEDDPDVQISWFFVNNVEVHTAQQTTHRE
DYNSTLRVVSALPIQHODWMSGKAFACAVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQV
TLTCMVTDMPEDIYVEWTNNGKTELNYKNTPEVLDSGYSYFMYSKLRVEKKNWVERNSYSCSVVHEGL
HNHHTTKSFSRTPGK

Fig. 7A

NEGS	PKRS	GSGS	EPRG	PGK
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Secretory Mu GDF-8 propeptide Mu IgG2a Fc
leader

MMQKLQMYVYIYLFMLIAAGPVDLNEGSEEREENVEKEGLCNACAWRQNTSYSRIEAIKIQLSKLRLET
APNISKDAIRQLLPRAAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIIITMPTESDFLMQADGKPKC
CFFKFSSKIQYNKVVAQQLWIYLRPVKTPTTVFVQILRLIKPMKDGTTRYTGIRSLKLDMSPGTGIWQSI
DVKTVLQNLWKQPESNLIGIEIKALDENGHDLA VTFPGPGEDGLNPFLEVKVTDTPKRSGSGSEPRGPTI
KPCPPCKCPAPNLEGGPSVFIFPPKIKDVLMSLSPIVTCVVDVSEDDPDVQISWFFVNNVEVHTAQQTQ
THREDYNSTLRVVSALPIQHODWMSGKAFACAVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMT
KKQVTLTCTVTDMPEDIYVEWTNNGKTELNYKNTPEVLDSGYSYFMYSKLRVEKKNWVERNSYSCSVV
HEGLHNHHTTKSFSRTPGK

Fig. 7B

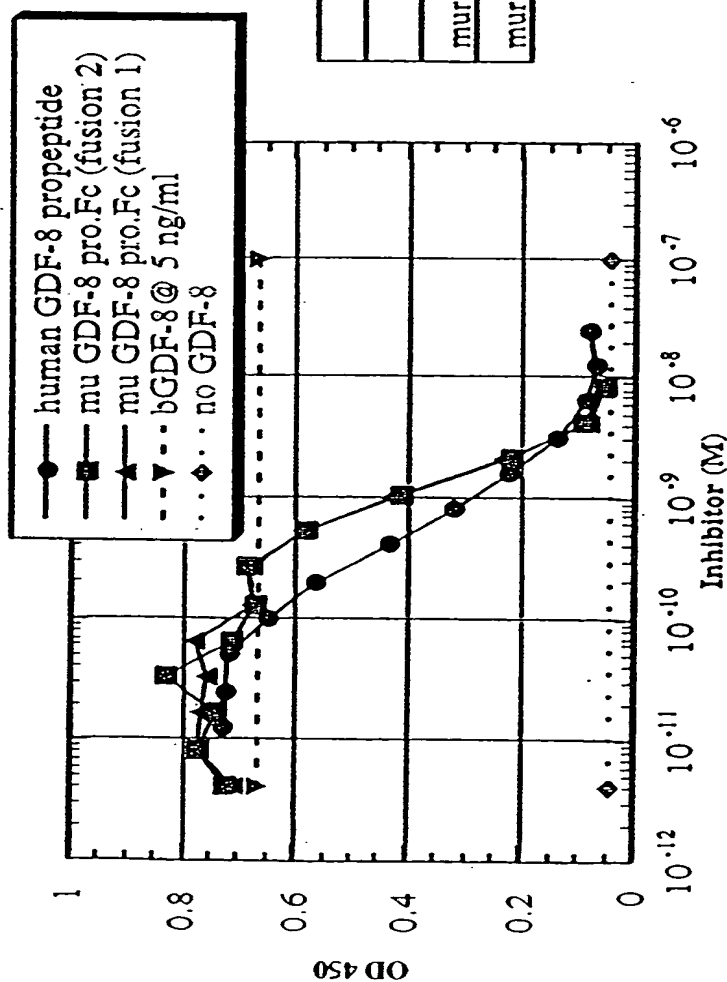


Fig. 8 A

Inhibitor	IC50 (M)
hu GDF-8 propeptide	6×10^{-10}
murine GDF-8 pro.Fc (Fusion 1)	1.3×10^{-9}
murine GDF-8 pro.Fc (Fusion 2)	1.3×10^{-9}

Fig. 8 B

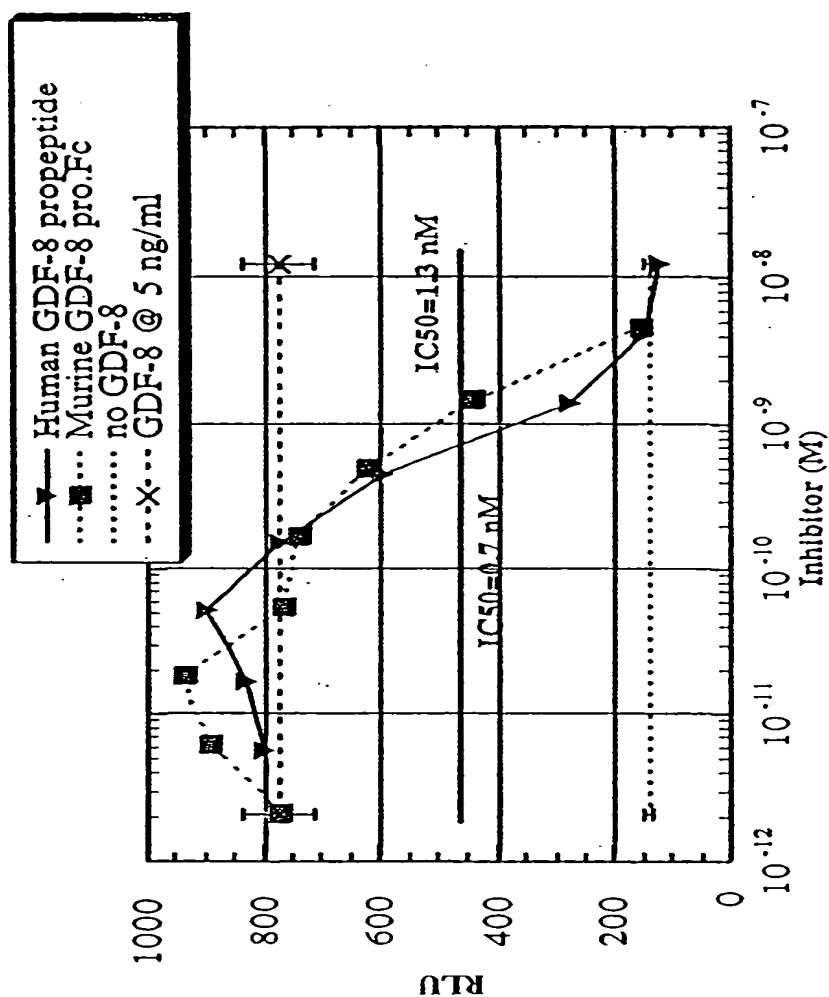


Fig. 9

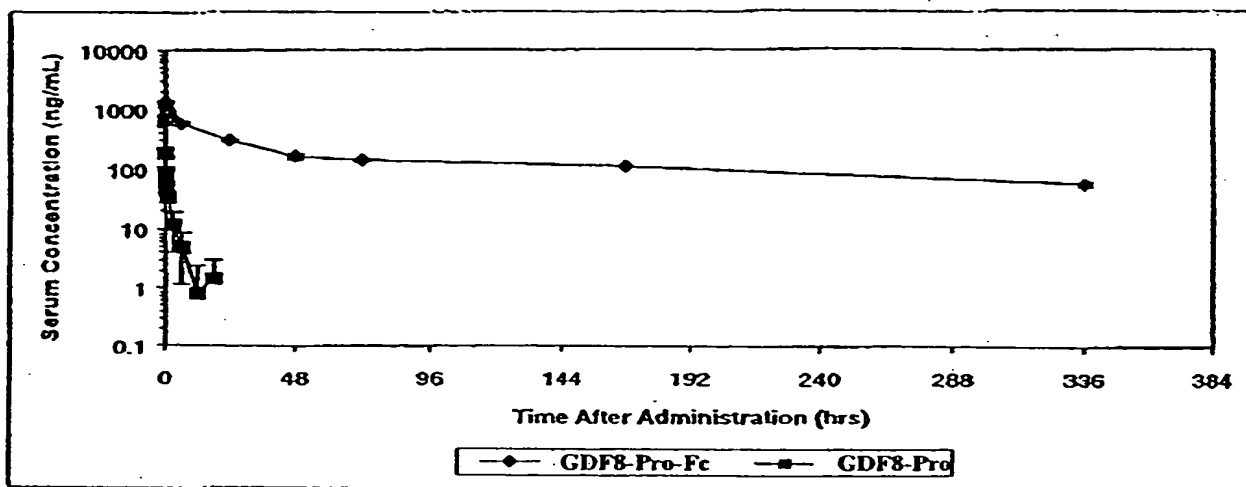


Fig. 10

20220804 16:41:20

Applicants: Neil M. Wolfman, *et al.*
For: Modified and Stabilized GDF
Propeptides and Uses Therefor
Docket No.: AM100384

	NENS	PKRS	EPKS	PGK
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Secretory Hu GDF-8 propeptide Hu IgG1 Fc
leader

MQKLQLCVYIYLFMLIVAGPVDLNNSENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQLSKLRLETAPN
ISKDVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIIITPTESDFLMQVDGKPKCCFFKF
SSKIQYNKVVKQQLWIYLRPVEPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMPGTGIWQSIDVKTVLQ
NWLKQPESNLGIKALDENGGHDLAVTFPGPGEDGLNPFLEVKVTDTPKRSEPKSCDKTHTCPCPAPELL
GGPSVFLFPPPKPDKTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI
AVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVCMHEALHNHYTQKSLSLSPGK

Fig. 11A

	NENS	PKRS	DKT	PGK
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Secretory Hu GDF-8 propeptide Hu IgG1 Fc mutated
 leader

MQKLQLCVYIYLFMLIVAGPVLDLNENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPN
 ISKDVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIIITMPTESDFLMQVDGKPKCCFFKF
 SSKIQYNKVVKAKQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMPGTGIWQSIDVKTVLQ
 NWLKQPESNLGIKALDENGGHDLAVTFPGPGEDGLNPFLVVKVTDTPKRSDKTHTCPPCPAPEALGAPSV
 FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNATKPREEQYNSTYRVVSVLTVHLQ
 DWLNGKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE
 SNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFVMSHEALTHYHTQKSLSLSPGK

Fig. 11B

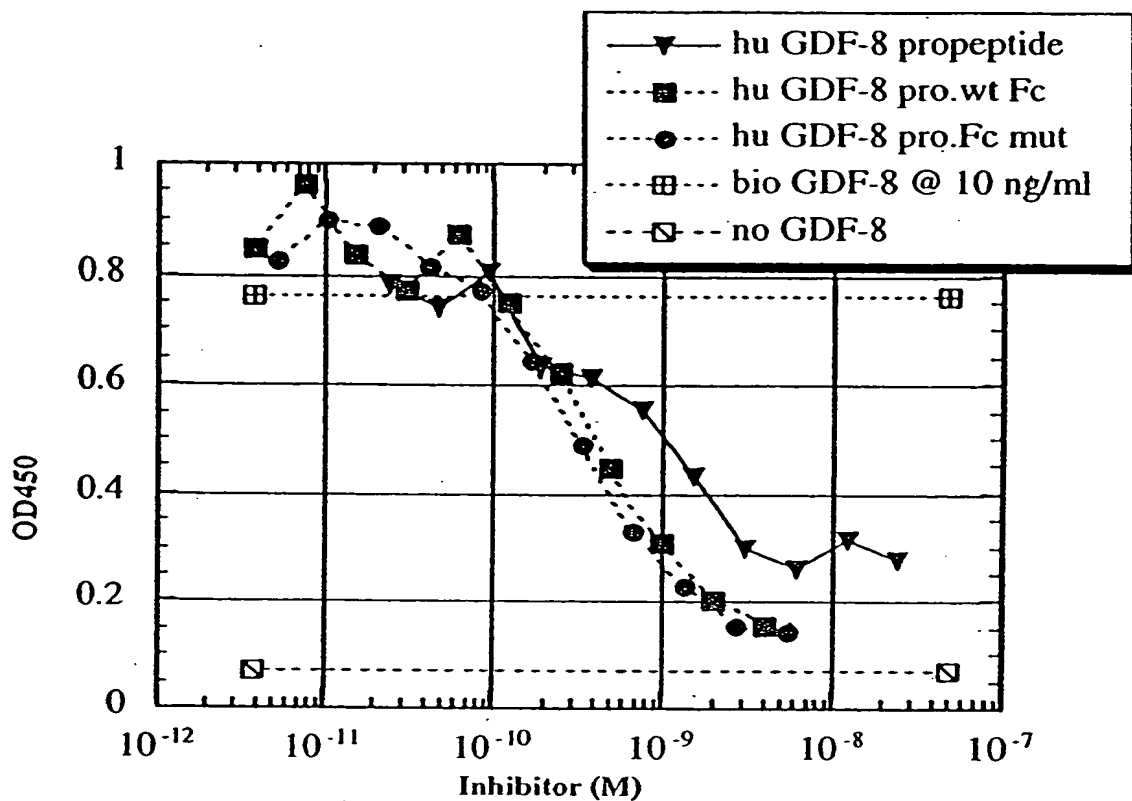


Fig. 12

Dissected Tissue Mass

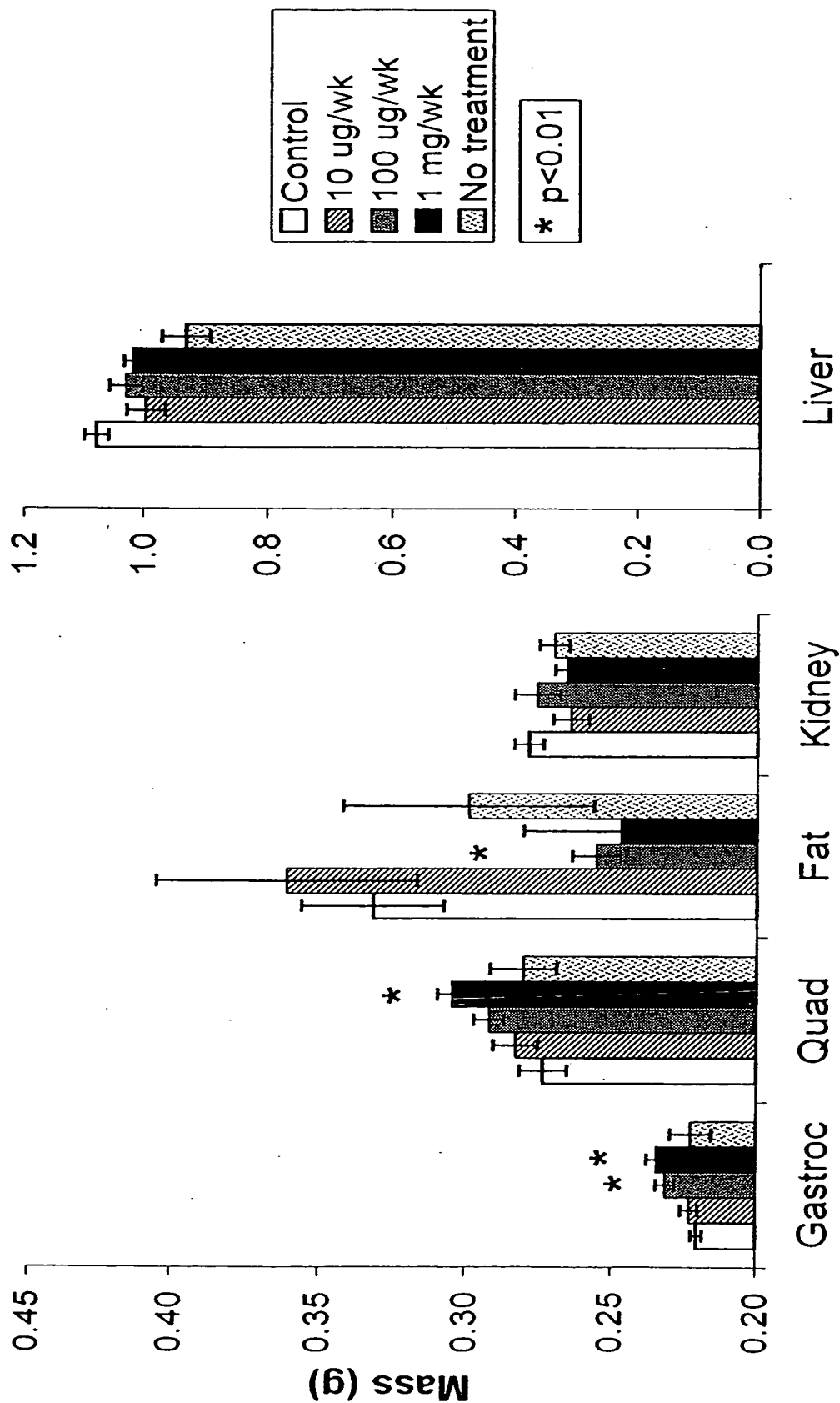


Figure 13

Fig. 14A

SEQ ID NO:1 Human GDF-8 precursor protein - protein
sequence

MQKLQLCVYIYLFMLIVAGPVDLNENSEQKENVEKEGLCNACTWRQNTKSS
RIEAIKIQILSKLRLETAPNISKDVIRQLLPKAPPLRELIDQYDVQRDDSS
DGSLEDDDYHATTETIITMPTESDFLMQVDGKPKCCFFKFSSKIQYNKVVK
AQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMPGTGIWQ
SIDVKTVLQNWLKQPESNLGIEIKALDENGHDLAVTFPGPGEDGLNPFLEV
KVTDTPKRSRRDFGLDCDEHSTESRCCRYPLTVDFEAFGWDWIIAPKRYKA
NYCSGECEFVFLQYPHTHLVHQANPRGSAGPCCTPTKMSPINMLYFNGKE
QIIYGKIPAMVVDRCGCS

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Fig. 14B

SEQ ID NO:2 Human GDF-8 precursor protein - DNA
sequence

ATGCAAAAAGCTGCAACTCTGTGTTTATATTTACCTGTTTATGCTGATTGT
TGCTGGTCCAGTGGATCTAAATGAGAACAGTGAGCAAAAAGAAAATGTGG
AAAAAGAGGGGCTGTGTAATGCATGTACTTGGAGACAAAACACTAAATCT
TCAAGAATAGAAGCCATTAAGATACAAATCCTCAGTAAACTTCGTCTGGA
AACAGCTCCTAACATCAGCAAAGATGTTATAAGACAACCTTTTACCCAAAG
CTCCTCCACTCCGGGAAGTATTGATCAGTATGATGTCCAGAGGGATGAC
AGCAGCGATGGCTCTTTGGAAGATGACGATTATCACGCTACAACGGAAAC
AATCATTACCATGCCTACAGAGTCTGATTTTCTAATGCAAGTGGATGGAA
AACCCAAATGTTGCTTCTTTAAATTTAGCTCTAAAATACAATACAATAAA
GTAGTAAAGGCCCAACTATGGATATATTTGAGACCCGTCGAGACTCCTAC
AACAGTGTTTGTGCAAATCCTGAGACTCATCAAACCTATGAAAGACGGTA
CAAGGTATACTGGAATCCGATCTCTGAAACTTGACATGAACCCAGGCACT
GGTATTTGGCAGAGCATTGATGTGAAGACAGTGTTGCAAAATTGGCTCAA
ACAACCTGAATCCAACCTTAGGCATTGAAATAAAAGCTTTAGATGAGAATG
GTCATGATCTTGCTGTAACCTTCCCAGGACCAGGAGAAGATGGGCTGAAT
CCGTTTTTTAGAGGTCAAGGTAACAGACACACCAAAAAGATCCAGAAGGGA
TTTTGGTCTTGACTGTGATGAGCACTCAACAGAATCACGATGCTGTCGTT
ACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATCGCT
CCTAAAAGATATAAGGCCAATTACTGCTCTGGAGAGTGTGAATTTGTATT
TTTACAAAATATCCTCATACTCATCTGGTACACCAAGCAAACCCCAGAG
GTTCAGCAGGCCCTTGCTGTACTCCACAAAGATGTCTCCAATTAATATG
CTATATTTTAATGGCAAAGAACAATAATATATGGGAAAATTCCAGCGAT
GGTAGTAGACCGCTGTGGGTGCTCA

Fig. 14C

SEQ ID NO:3 Human mature GDF-8 - protein sequence

DFGLDCDEHSTESRCCRYPLTVDFEAFGWDWIIAPKRYKANYCSGECEFVF
LQKYPHTHLVHQANPRGSAGPCCTPTKMSPINMLYFNGKEQIIYGKIPAMV
VDRCGCS

Fig. 14D

SEQ ID NO:4 Human mature GDF-8 - DNA sequence

GATTTTGGTCTTGACTGTGATGAGCACTCAACAGAATCACGATGCTGTCG
TTACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATCG
CTCCTAAAAGATATAAGGCCAATTACTGCTCTGGAGAGTGTGAATTTGTA
TTTTTACAAAAATATCCTCATACTCATCTGGTACACCAAGCAAACCCCAG
AGGTTTCAGCAGGCCCTTGCTGTACTCCCACAAAGATGTCTCCAATTAATA
TGCTATATTTTAATGGCAAAGAACAAATAATATATGGGAAAATTCCAGCG
ATGGTAGTAGACCGCTGTGGGTGCTCA

Fig.14E

SEQ ID NO:5 Human GDF-8 propeptide - protein
sequence

NENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPNISK
DVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTES
DFLMQVDGKPKCCFFKFSSKIQYNKVKAQLWIYLRPVETPTTVFVQILRL
IKPMKDGTRYTGIRSLKLDMNPGTGIWQSIDVKTVLQNLWKQPESNLGIEI
KALDENGHDLAVTFPGPGEDGLNPFLEVKVTDTPKRSRR

Fig. 14F

SEQ ID NO:6 Human GDF-8 propeptide - DNA sequence

AATGAGAACAGTGAGCAAAAAGAAAATGTGGAAAAAGAGGGGCTGTGTAAT
GCATGTACTTGGAGACAAAACACTAAATCTTCAAGAATAGAAGCCATTAAG
ATACAAATCCTCAGTAACTTCGTCTGGAAACAGCTCCTAACATCAGCAAA
GATGTTATAAGACAACTTTTACCCAAAGCTCCTCCACTCCGGGAAGTGATT
GATCAGTATGATGTCCAGAGGGATGACAGCAGCGATGGCTCTTTGGAAGAT
GACGATTATCACGCTACAACGGAAACAATCATTACCATGCCTACAGAGTCT
GATTTTCTAATGCAAGTGGATGGAAAACCCAAATGTTGCTTCTTTAAATTT
AGCTCTAAAATACAATAACAATAAAGTAGTAAAGGCCCAACTATGGATATAT
TTGAGACCCGTCGAGACTCCTACAACAGTGTTTGTGCAAATCCTGAGACTC
ATCAAACCTATGAAAGACGGTACAAGGTATACTGGAATCCGATCTCTGAAA
CTTGACATGAACCCAGGCACTGGTATTTGGCAGAGCATTGATGTGAAGACA
GTGTTGCAAAATTGGCTCAAACAACCTGAATCCAACCTTAGGCATTGAAATA
AAAGCTTTAGATGAGAATGGTCATGATCTTGCTGTAACTTCCCAGGACCA
GGAGAAGATGGGCTGAATCCGTTTTTAGAGGTCAAGGTAACAGACACACCA
AAAAGATCCAGAAGG

Fig. 14G

SEQ ID NO:7 Human BMP-11 precursor protein -
protein sequence

MVLAAPLLLGFLLLALELRPRGEAAEGPAAAAAAAAAAAAAGVGGERSRP
APVAPEPDGCPVCVWRQHSRELRLSEIKSQILSKLRLKEAPNISREVVKQ
LLPKAPPLQQILDLHDFQGDALQPEDFLEEDEYHATTETVISMAQETDPAV
QTDGSPLCCHFHFSPKVMFTKVLKAQLWVYLRPVPRPATVYLQILRLKPLT
GEGTAGGGGGGRRHIRIRSLKIELHSRSGHWQSIDFKQVLHSWFRQPQSNW
GIEINAFDPSGTDLAVTSLGPGAEGLHPFMELRVLENTKRSRRNLGLDCDE
HSSESRCRYPLTVDFEAFGWDWIIAPKRYKANYCSGQCEYMFQMYPHTH
LVQQANPRGSAGPCCTPTKMSPINMLYFNDKQQIIYGKIPGMVVDRCGCS

Fig. 14H

SEQ ID NO:8 Human BMP-11 precursor protein - DNA
sequence

ATGGTGCTCGCGGCCCCGCTGCTGCTGGGCTTCCTGCTCCTCGCCCTGGA
GCTGCGGCCCCGGGGGGAGGCGGCCGAGGGCCCCGCGGCGGCGGCGGCGG
CGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG
CCAGCCCCGTCCGTGGCGCCCCGAGCCGGACGGCTGCCCCGTGTGCGTTTG
GCGGCAGCACAGCCGCGAGCTGCGCCTAGAGAGCATCAAGTCGCAGATCT
TGAGCAAACCTGCGGCTCAAGGAGGCGCCCAACATCAGCCGCGAGGTGGTG
AAGCAGCTGCTGCCCAAGGCGCCGCGCTGCAGCAGATCCTGGACCTACA
CGACTTCCAGGGCGACGCGCTGCAGCCCCGAGGACTTCCTGGAGGAGGACG
AGTACCACGCCACCACCGAGACCGTCATTAGCATGGCCCAGGAGACGGAC
CCAGCAGTACAGACAGATGGCAGCCCTCTCTGCTGCCATTTTCACTTCAG
CCCCAAGGTGATGTTTACAAAGGTAAGGAGGAGGAGGAGGAGGAGGAGGAG
TACGGCCTGTACCCCGCCAGCCACAGTCTACCTGCAGATCTTGCGACTA
AAACCCCTAACTGGGGAAGGGACCGCAGGGGGAGGGGGCGGAGGCCGGCG
TCACATCCGTATCCGCTCACTGAAGATTGAGCTGCACTCACGCTCAGGCC
ATTGGCAGAGCATCGACTTCAAGCAAGTGCTACACAGCTGGTTCCGCCAG
CCACAGAGCAACTGGGGCATCGAGATCAACGCCTTTGATCCCAGTGGCAC
AGACCTGGCTGTCACCTCCCTGGGGCCGGGAGCCGAGGGGCTGCATCCAT
TCATGGAGCTTCGAGTCCTAGAGAACACAAAACGTTCCCGGCGGAACCTG
GGTCTGGACTGCGACGAGCACTCAAGCGAGTCCCGCTGCTGCCGATATCC
CCTCACAGTGGACTTTGAGGCTTTTCGGCTGGGACTGGATCATCGCACCTA
AGCGCTACAAGGCCAACTACTGCTCCGGCCAGTGCGAGTACATGTTTCATG
CAAAAATATCCGCATACCCATTTGGTGCAGCAGGCCAATCCAAGAGGCTC
TGCTGGGCCCTGTTGTACCCCCACCAAGATGTCCCAATCAACATGCTCT
ACTTCAATGACAAGCAGCAGATTATCTACGGCAAGATCCCTGGCATGGTG
GTGGATCGCTGTGGCTGCTCT

Fig. 14I

SEQ ID NO:9 Human BMP-11 mature - protein sequence

NLGLDCDEHSSESRCRYPLTVDFEAFGWDWIIAPKRYKANYCSGQCEYMF
MQKYPHTHLVQQANPRGSAGPCCTPTKMSPINMLYFNDKQQIIYGKIPGMV
VDRCGCS

Fig. 14J

SEQ ID NO:10 Human BMP-11 mature - DNA sequence

AACCTGGGTCTGGACTGCGACGAGCACTCAAGCGAGTCCCGCTGCTGCCG
ATATCCCCTCACAGTGGACTTTGAGGCTTTCGGCTGGGACTGGATCATCG
CACCTAAGCGCTACAAGGCCAACTACTGCTCCGGCCAGTGCGAGTACATG
TTCATGCAAAAATATCCGCATACCCATTTGGTGCAGCAGGCCAATCCAAG
AGGCTCTGCTGGGCCCTGTTGTACCCCCACCAAGATGTCCCCAATCAACA
TGCTCTACTTCAATGACAAGCAGCAGATTATCTACGGCAAGATCCCTGGC
ATGGTGGTGGATCGCTGTGGCTGCTCT

Fig. 14K

SEQ ID NO:11 Human BMP-11 propeptide - protein
sequence

AEGPAAAAAAAAAAAAAGVGGERSSRPAPSVAPEPDGCPVCVWRQHSREL
LESIKSQILSKLRLKEAPNISREVVKQLLPKAPPLQQILDHDFQGDALQP
EDFLEEDEYHATTETVISMAQETDPAVQTDGSPLCCHFHFSPKVMFTKVLK
AQLWVYLRPVPRPATVYLQILRLKPLTGEGTAGGGGGGRRHIRIRSLKIEL
HSRSGHWQSIDFKQVLHSWFRQPQSNWGIEINAFDPSGTDLAVTSLGPGAE
GLHPFMELRVLENTKRSRR

Fig. 14O

SEQ ID NO:15 Human IgG1-Fc - protein sequence

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGK

Fig. 14P

SEQ ID NO:16 Human IgG1-Fc modified - protein
sequence

DKTHTCPPCPAPEALGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPGK

SECRET